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Pharmacokinetic and Toxicological Characterization of Tetrandrine Using *in silico* ADMET Modelling

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ABSTRACT

Tetrandrine, a bis-benzylisoquinoline alkaloid from Stephania tetrandra, is widely investigated as a multitarget anticancer and chemosensitizing candidate, but its developability depends on a clear pharmacokinetic and safety profile. This study assessed tetrandrine using an integrated in silico ADMET workflow (SwissADME, pkCSM, and ADMETlab 3.0) and predicted acute toxicity with GUSAR. Tetrandrine showed high lipophilicity (consensus LogP 5.49; 3.73-6.66 across models) and very low aqueous solubility (ESOL LogS -8.02; Ali LogS -7.76; SILICOS-IT LogS -10.8; pkCSM solubility -3.886 log mol/L), with moderate passive permeability (Caco-2 0.43 log Papp). The BOILED-Egg model indicated a high probability of intestinal absorption with limited blood-brain barrier (BBB) penetration, consistent with low BBB permeability (LogBB -0.618) and low CNS permeability (logPS -2.27). Distribution estimates suggested moderate tissue distribution (Vd -0.624, log scale) and a measurable free fraction in plasma (fu 0.358). P-glycoprotein classification differed between tools, but pkCSM consistently predicted P-gp I/II inhibition. Metabolism models predicted tetrandrine as a substrate of CYP1A2, CYP2C9, CYP2C19, CYP2B6, and CYP3A4, with low inhibitory potential; CYP2D6 substrate status was tool-dependent. Elimination parameters indicated moderate clearance (0.71 log mL/min/kg; 9.238 mL/min/kg) and a predicted half-life of 2.567 h, with no OCT2 substrate liability. GUSAR predicted route-dependent LD50 values of 65.4 mg/kg (IV), 70.9 mg/kg (IP), 121.8 mg/kg (SC), and 708.3 mg/kg (oral). Overall, tetrandrine appears pharmacokinetically challenging, supporting the need for solubility-enhancing formulations and focused non-clinical safety studies.

Keywords: Pharmacokinetics; *in silico* ADMET; Toxicity; Chemosensitizing agent; Breast cancer.

INTRODUCTION

Tetrandrine is a bis-benzylisoquinoline alkaloid isolated mainly from *Stephania tetrandra* that has long been used in East Asian medicine for inflammatory and cardiovascular disorders and more recently has been intensively investigated as a multi-target small molecule for modern pharmacotherapy. Beyond its classical calcium channel blocking and immunomodulatory properties, tetrandrine displays broad anticancer activity by

modulating cell-cycle progression, apoptosis, autophagy, angiogenesis, and multidrug resistance pathways across diverse tumor types, including breast cancer (1, 2). However, successful translation of such pleiotropic pharmacology into safe and effective therapies critically depends on a clear understanding of the compound's pharmacokinetic (PK) behavior and toxicity profile.

Breast cancer remains the most commonly diagnosed malignancy among women worldwide, and triple-negative breast cancer (TNBC) continues to be associated with poor prognosis, chemoresistance, and limited targeted options. In this context, natural products with chemosensitizing and stem cell modulating effects are being explored as adjuncts to standard chemotherapy. Recent experimental work has shown that tetrandrine can inhibit cancer stem cell characteristics and epithelial-mesenchymal transition in TNBC models via modulation of SOD1/ROS signaling, thereby attenuating aggressive, therapy-resistant phenotypes (3, 4). Bhagya et al. (2020) reported that the combination of tetrandrine with cisplatin exerts synergistic cytotoxicity against TNBC cells, supporting its potential role as a chemosensitizer in breast cancer therapy. These findings reinforce the need to delineate tetrandrine's PK and safety characteristics under clinically relevant exposure scenarios if it is to be repositioned or optimized for breast cancer management (5).

Despite its promising pharmacology, tetrandrine exhibits several unfavorable biopharmaceutical properties. It is a highly lipophilic quaternary ammonium compound with very low aqueous solubility at physiological pH, which contributes to variable absorption and limited oral bioavailability (1, 6). Preclinical PK studies in rodents have demonstrated extensive tissue distribution with a large apparent volume of distribution, prolonged residence in organs such as lung, liver, spleen, and kidney, and relatively slow systemic elimination, suggesting the potential for tissue accumulation during repeated dosing. Quantitative MALDI imaging and LC–MS/MS analyses have further revealed heterogeneous, region-specific distributions of tetrandrine and its metabolites in the lung and liver, which may underpin organ-specific toxicities (7). Safety concerns also warrant systematic evaluation. Experimental toxicology has reported acute and sub-chronic toxicity at higher doses, including pulmonary injury linked to CYP3A-mediated bioactivation in the lung, hepatocellular dysfunction associated with reactive oxygen species and mitochondrial impairment, and nephrotoxicity in comparative models.

Given the growing interest in tetrandrine as an anticancer and chemosensitizing agent, including in breast cancer, a coherent appraisal of its pharmacokinetic behavior and toxicity risk using state-of-the-art prediction platforms is timely. The present study therefore aims to characterize the pharmacokinetic and toxicity profile of tetrandrine by combining in silico ADMET modelling (ADMETlab 3.0, pkCSM, SwissADME) with existing experimental evidence, with particular emphasis on parameters relevant to systemic exposure, organ distribution, and safety margins in oncology. By aligning with the pharmacokinetics and toxicokinetics, this work is expected to provide a rational basis for future formulation strategies and for the safe repositioning of tetrandrine, including as a potential adjunct in breast cancer therapy.

MATERIALS & METHODS

Tetrandrine compound were obtained using the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The SMILES sequence of each molecule was entered into pKCSM (https://biosig.lab.uq.edu.au/pkcsm/prediction) to evaluate pharmacokinetic potential, as well as into Swiss-ADME (https://swissadme.ch/) and ADMETlab 3.0 (https://admetlab3.scbdd.com/server/screening), and toxicity was obtained from

GUSAR (General Unrestricted Structure-Activity Relationships) (https://way2drug.com/Gusar/acutoxpredict.html) (8).

RESULT

In Silico Absorption

Tetrandrine showed a markedly lipophilic profile across SwissADME predictors, with LogP values ranging from 3.73 (MLOGP) to 6.66 (XLOGP3) and a consensus LogP of 5.49, indicating high membrane affinity but potential dissolution limitations. Consistently, aqueous solubility was predicted to be very low: ESOL LogS was −8.02 (9.57×10^{-9} mol/L) and Ali LogS was −7.76 (1.73×10^{-8} mol/L), both classified as poorly soluble, while SILICOS-IT predicted an even lower LogS of −10.8 (1.57×10^{-11} mol/L), classified as insoluble. pkCSM also indicated low solubility (−3.886 log mol/L). The predicted Caco-2 permeability was 0.43 (log Papp in 10^{-6} cm/s), supporting passive permeability potential. For P-glycoprotein (P-gp) interaction, SwissADME predicted tetrandrine as a non-substrate, whereas pkCSM predicted it as a substrate; however, pkCSM consistently predicted P-gp I and P-gp II inhibitory activity.

Table 1. In silico absorption parameters of tetrandrine predicted

Parameter		Value	
logP		Log Po/w (iLOGP)	5.23
		Log Po/w (XLOGP3)	6.66
		Log Po/w (WLOGP)	5.75
		Log Po/w (MLOGP)	3.73
		Log Po/w (SILICOS-IT)	6.06
		Consensus Log Po/w	5.49
Solubility in water		Log S (ESOL)	-8.02
		Solubility	9.57e-09 mol/L
		Class	Poorly Soluble
		Log S (Ali)	-7.76
		Solubility	1.73e-08 mol/L
		Class	Poorly Soluble
		Log S (SILICOS-IT)	-10.8
		Solubility	1.57e-11 mol/L
		Class	Insoluble
		-3.886 (log mol/L)	
Passive absorption	Caco-2	0.43 (log Papp in 10^{-6} cm/s)	
P-glycoprotein	P-gp substrate	No	
		Yes	
	P-gp I inhibitor	Yes	
	P-gp II inhibitor	Yes	

Distribution and exposure of the central nervous system

Table 2. Predicted distribution and central nervous system penetration of tetrandrine.

Parameter		Value
Volume of Distribution (Vd)		-0.624
Fraction unbound (Fu) in Plasma		0.358
Blood-Brain Barrier	BBB permeant	No
	BBB permeability (LogBB)	-0.618
	CNS permeability (logPS)	-2.27

Distribution modelling (pkCSM) estimated a volume of distribution (Vd) of −0.624 (log scale) and a plasma fraction unbound (Fu) of 0.358, suggesting moderate protein binding with a measurable free fraction in circulation. Regarding CNS disposition, SwissADME predicted tetrandrine as non–BBB permeant. pkCSM further indicated

low BBB permeability (LogBB −0.618) and low CNS permeability (logPS −2.27), consistent with limited central exposure.

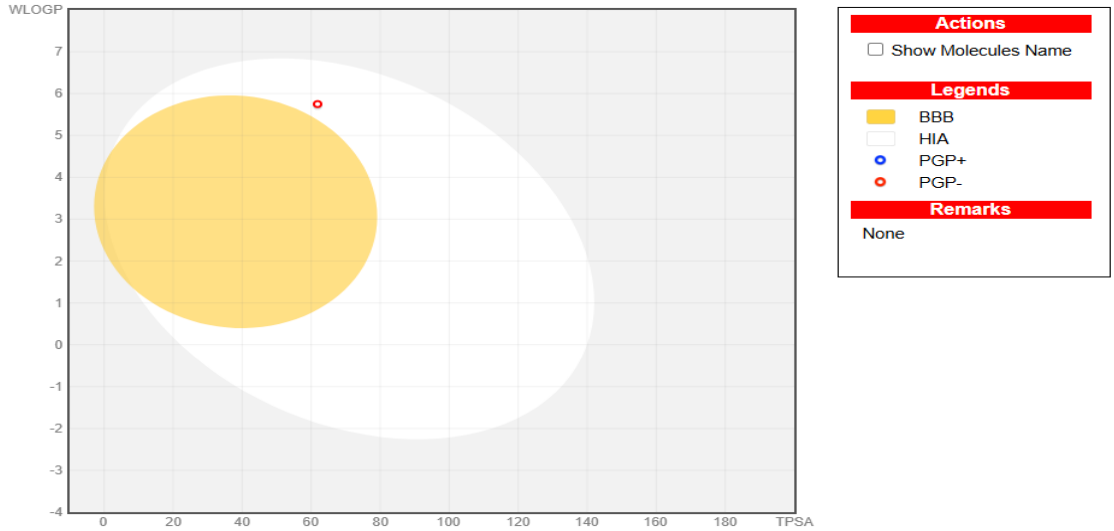

Figure 1. BOILED-Egg plot of tetrandrine predicting gastrointestinal absorption and blood–brain barrier permeation.

Tetrandrine was located within the HIA (white) region of the SwissADME BOILED-Egg plot, indicating a high probability of intestinal absorption, while remaining outside the BBB (yellow) region, suggesting limited blood–brain barrier permeation. The compound was classified as PGP−, consistent with a predicted non-substrate profile for P-glycoprotein in this model.

Metabolic liability and drug interaction potential

Table 3. Prediction of metabolic risk of tetrandrine compounds.

Parameter	Value
CYP1A2 substrate	Yes
CYP1A2 inhibitor	No
	No
	No
CYP2C9 substrate	Yes
CYP2C9 inhibitor	No
	No
	No
CYP2C19 Substrate	Yes
CYP2C19 inhibitor	No
	No
	No
CYP2D6 substrate	No
	Yes
CYP2D6 inhibitor	No
	No
	No
CYP3A4 substrate	Yes
	Yes
CYP3A4 inhibitor	No
	No
	No
CYP2B6 substrate	Yes
CYP2B6 inhibitor	No

Multiple models suggested that tetrandrine may undergo extensive hepatic metabolism. ADMETlab 3.0 predicted tetrandrine as a substrate of CYP1A2, CYP2C9, CYP2C19, and CYP2B6, while both pkCSM and ADMETlab 3.0 indicated CYP3A4 substrate status. For CYP2D6, predictions differed between tools (non-substrate in pkCSM but substrate in ADMETlab 3.0), highlighting model-dependent uncertainty for this isoform. Across platforms, tetrandrine was consistently predicted as a non-inhibitor of key CYP isoforms (including CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A4).

Excretion and elimination parameters

Table 4. Predicted excretion and elimination parameters of tetrandrine

Parameter	Value
Total Clearance	0.71 (log mL/min/kg)
	9.238 (mL/min/kg)/
Half-live	2.567 (hours)
Renal OCT2 substrate	No

Elimination modelling predicted a total clearance of 0.71 (log mL/min/kg) in pkCSM, while ADMETlab 3.0 estimated clearance at 9.238 mL/min/kg and a half-life of 2.567 hours. pkCSM predicted tetrandrine as not being a renal OCT2 substrate, suggesting OCT2-mediated renal secretion is unlikely to be a major elimination pathway.

In silico acute toxicity profile

Acute toxicity modelling using GUSAR produced route-dependent LD_{50} estimates for tetrandrine. The predicted LD_{50} values were 70.920 mg/kg (intraperitoneal), 65.400 mg/kg (intravenous), 708.300 mg/kg (oral), and 121.800 mg/kg (subcutaneous), indicating substantially higher tolerated doses via the oral route compared with parenteral administration.

Table 5. LD_{50} prediction using GUSAR (mg/kg)

Compound Name	IP	IV	ORAL	SC
Tetrandrine	70.920[d]	65.400[c]	708.300[c]	121.800[d]

[a]**Non-toxic compound;** [b]**Class 5 compound;** [c]**Class 4 compound;** [d]**Class 3 compound;** [e]**Class 2 compound.**

DISCUSSION

SwissADME predicted tetrandrine to be highly lipophilic, with individual logP values ranging from 3.73 (MLOGP) to 6.66 (XLOGP3) and a consensus logP of 5.49, indicating a strongly hydrophobic molecule. Water solubility was consistently very low: ESOL and Ali models estimated logS values of −8.02 and −7.76, corresponding to aqueous solubilities in the order of 10^{-8} mol/L and classifying tetrandrine as "poorly soluble," while the SILICOS-IT model gave logS −10.8, categorized as "insoluble." These data confirm that tetrandrine has an unfavorable dissolution profile for oral formulations, which is consistent with the poor aqueous solubility and low oral bioavailability summarized by Luan and colleagues in their pharmacokinetic review of tetrandrine (1), supported by a moderate Caco-2 permeability of 0.43 log Papp (10^{-6} cm/s) (Table 1). This pattern of poor solubility but good predicted permeability is typical of highly lipophilic Biopharmaceutics Classification System (BCS) class II-like compounds, in which dissolution rather than membrane permeation becomes the primary limitation to oral exposure. Daina et al. (2023) showed that SwissADME reliably flags such solubility-permeability trade-offs for drug-like small molecules, supporting the use of these predictions for early formulation planning (9). The interaction of tetrandrine with P-glycoprotein (P-gp) appeared model-dependent. SwissADME predicted that

tetrandrine is not a P-gp substrate, whereas pkCSM classified it as a P-gp substrate and simultaneously predicted that it acts as both a P-gp I and a P-gp II inhibitor. These seemingly conflicting outputs likely reflect limitations of classification thresholds rather than true biological incompatibility, because experimental pharmacokinetic work by Dai et al. demonstrated that intraperitoneal tetrandrine achieved micromolar plasma concentrations sufficient to reverse P-gp mediated multidrug resistance (MDR) in mice without significantly altering doxorubicin pharmacokinetics (10). Together, the in silico data and in vivo MDR studies suggest that tetrandrine behaves primarily as a P-gp modulator/inhibitor with possible partial substrate behavior, which may contribute both to its chemosensitizing properties and to variability in its oral bioavailability.

The predicted log volume of distribution (Vd) for tetrandrine was −0.624 L/kg, suggesting a moderate distribution into tissues, while the fraction unbound in plasma (fu) was estimated at 0.358, indicating that approximately one-third of circulating tetrandrine remains free rather than protein-bound. At first glance, these values may appear somewhat conservative for a highly lipophilic alkaloid. However, they are not incompatible with published pharmacokinetic observations, where tetrandrine exhibits rapid distribution to highly perfused organs but also shows relatively limited free fraction and considerable inter-individual variability (1). Both SwissADME and pkCSM predicted limited penetration of the blood-brain barrier (BBB). Tetrandrine was classified as "non-BBB permeant" by SwissADME, while pkCSM predicted a logBB of −0.618 and a CNS permeability (logPS) of −2.27, consistent with negligible central nervous system exposure (Table 2). At the same time, moderate predicted tissue distribution and limited BBB penetration imply that tetrandrine's therapeutic window will be driven largely by peripheral target engagement (e.g., tumor, lung, or immune tissues) rather than central targets. This is particularly relevant when tetrandrine is considered as an adjuvant in cancer therapy or as an antiviral or anti-fibrotic agent, where high local concentrations in lung and liver are desirable but sustained CNS exposure is unnecessary (11). According to the SwissADME BOILED-Egg model, tetrandrine (red hollow point) displays a high lipophilicity (WLOGP 5.75) with a TPSA of around 60 Å². Its position within the white area indicates a high probability of efficient gastrointestinal absorption, whereas its location outside the yellow region suggests limited ability to cross the blood–brain barrier. The hollow red symbol further denotes that tetrandrine is predicted to be a non-substrate of P-glycoprotein. Overall, this profile supports tetrandrine as a promising orally administered candidate with restricted penetration into the central nervous system (Figure 1).

The integrated metabolism panel showed that tetrandrine is predicted to be a substrate for multiple cytochrome P450 (CYP) isoforms. ADMETlab 3.0 indicated substrate status for CYP1A2, CYP2C9, CYP2C19, CYP2B6, and CYP3A4, while pkCSM and SwissADME agreed that tetrandrine is not a significant inhibitor of these isoenzymes. Only CYP2D6 status was inconsistent between tools, with ADMETlab 3.0 predicting tetrandrine as a substrate and pkCSM predicting it is not (Table 3). These in silico findings correlate well with mechanistic studies that demonstrated that tetrandrine undergoes metabolic activation in mouse lung and human liver microsomes to form a reactive quinone-methide metabolite, with CYP3A4 and CYP3A5 identified as the main enzymes responsible (12). Further showed that reactive oxygen species generated by cytochrome P450, particularly CYP2E1, mediate tetrandrine-induced mitochondrial dysfunction in rat hepatocytes. Together, these data support the in silico prediction that tetrandrine is extensively metabolized by hepatic CYPs, particularly within the CYP3A subfamily, with additional contribution from other

isoforms. Importantly, pkCSM and SwissADME uniformly predicted that tetrandrine is not a clinically relevant inhibitor of CYP1A2, CYP2C9, CYP2C19, CYP2D6, or CYP3A4. This agrees with the pharmacokinetic interaction study reported by Dai et al., in which tetrandrine at doses sufficient to reverse MDR did not significantly alter the clearance or AUC of doxorubicin in mice and had minimal impact on CYP3A4 activity at concentrations below 25 μM (10). These observations suggest that tetrandrine is more likely to be a victim rather than a perpetrator of CYP-mediated drug interactions, a point that is particularly relevant when co-administered with strong CYP3A indsucers or inhibitors in oncology or antiviral regimens. From a development perspective, the broad CYP substrate profile combined with low predicted inhibitory potency implies a complex metabolic clearance pattern but a relatively low risk of clinically significant CYP-based inhibition.

The excretion module predicted a total clearance of 0.71 log mL/min/kg by pkCSM and 9.238 mL/min/kg by ADMETlab 3.0, indicating a moderate systemic clearance for tetrandrine (Table 4). The predicted elimination half-life from ADMETlab 3.0 was 2.567 h, and tetrandrine was not classified as a substrate of renal OCT2, suggesting that renal tubular secretion is unlikely to be a major elimination pathway. Tetrandrine is a compound with low oral bioavailability and a relatively short elimination half-life, requiring repeated dosing or modified-release formulations to maintain therapeutic levels (1, 11). These experimental observations are compatible with the in silico predictions: a moderate clearance and a short to intermediate half-life imply that systemic exposure will be limited unless solubility and first-pass metabolism are addressed. Structural modification and nanocarrier-based delivery systems can partially overcome these pharmacokinetic limitations, a conclusion that is strongly supported by the current prediction set (6).

Clinically, a moderate clearance with limited renal contribution suggests that hepatic impairment and co-administration of CYP3A modulators may have a greater impact on tetrandrine exposure than reductions in renal function. However, because tetrandrine is also prone to tissue accumulation in the lung and liver, as shown in animal toxicity and biodistribution studies, careful dose escalation and therapeutic monitoring are still warranted (1, 12, 13).

Using GUSAR, the predicted rat LD_{50} values for tetrandrine (mg/kg) differed substantially across routes of administration: 65.4 mg/kg for intravenous (IV), 70.9 mg/kg for intraperitoneal (IP), 121.8 mg/kg for subcutaneous (SC), and 708.3 mg/kg for oral dosing. These predictions indicate a high acute toxicity risk for parenteral routes, with substantially lower predicted acute toxicity by the oral route. When mapped onto Globally Harmonized System (GHS) categories, the predicted oral LD_{50} falls within the range typically classified as category 4 (500–2000 mg/kg), whereas IV and IP predictions suggest a more hazardous profile (Table 5). These in silico predictions are in good agreement with experimental toxicity. Jin et al. showed that a single IP dose of 150 mg/kg tetrandrine in CD-1 mice induced pronounced pulmonary injury, characterized by alveolar hemorrhage and marked elevation of lactate dehydrogenase in bronchoalveolar lavage fluid (12). Reported mitochondria-mediated apoptosis in rat primary hepatocytes at micromolar concentrations of tetrandrine, and CYP-mediated reactive oxygen species, particularly via CYP2E1, trigger mitochondrial dysfunction and hepatotoxicity (14, 15). Sub-chronic IV dosing in BALB/c mice also produced dose-dependent hepatic and pulmonary changes, underscoring the need for cautious parenteral use (13). Taken together, the GUSAR-derived LD_{50} estimates and the available in vivo data converge on the conclusion that tetrandrine carries a significant risk of acute and cumulative

toxicity when administered systemically at high doses, particularly by IV or IP routes. Nevertheless, the relatively higher predicted oral LD_{50}, combined with its long history of clinical use in China for silicosis and inflammatory conditions, suggests that careful dose individualization and therapeutic monitoring can provide an acceptable safety margin in appropriately selected patients (1, 13).

CONCLUSION

This in silico evaluation shows that tetrandrine is a highly lipophilic compound with very low aqueous solubility, good predicted intestinal permeability, and moderate tissue distribution with minimal brain penetration. It undergoes extensive hepatic metabolism, predominantly via CYP3A isoforms, and displays moderate clearance with a relatively short elimination half-life. GUSAR-predicted LD_{50} values and published in vivo data together indicate a narrow safety margin for parenteral administration and a comparatively wider, but still limited, margin for oral use, with liver and lung emerging as key target organs for toxicity. Overall, tetrandrine can be considered a pharmacokinetically challenging molecule with a restricted therapeutic window. Its further development will require strategies to enhance solubility and systemic exposure, cautious dose optimization, and focused non-clinical safety studies, particularly when tetrandrine is proposed as an adjuvant or primary agent in cancer and other chronic diseases.

Declaration by Authors

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REFERENCES

1. Luan F, He X, Zeng N. Tetrandrine: a review of its anticancer potentials, clinical settings, pharmacokinetics, and drug delivery systems. *J Pharm Pharmacol.* 2020;72(11):1491-1512. doi:10.1111/jphp.13339.
2. Liu T, Liu X, Li W, Li C, Su Q, Yang J, et al. Tetrandrine, a Chinese plant-derived alkaloid, is a potential candidate for cancer chemotherapy. Oncotarget. 2016;7(26):40800–40815. doi:10.18632/oncotarget.8315
3. Liu T, Li K, Zhang Z, Peng J, Yang J, Law BYK, et al. Tetrandrine inhibits cancer stem cell characteristics and epithelial to mesenchymal transition in triple-negative breast cancer via SOD1/ROS signaling pathway. Am J Chin Med. 2023;51(2):425–444. doi:10.1142/S0192415X23500222
4. Błaszczak E, Miziak P, Odrzywolski A, Baran M, Gumbarewicz E, Stepulak A. Triple-negative breast cancer progression and drug resistance in the context of epithelial–mesenchymal transition. Cancers (Basel). 2025;17(2):228. doi:10.3390/cancers17020228
5. Bhagya N, Prabhu A, Rekha PD, Chandrashekar KR. Combination of tetrandrine and cisplatin synergises cytotoxicity and apoptosis in triple negative breast cancer. Synergy. 2020; 10:100063. doi: 10.1016/j.synres.2020.100063.
6. Mo L, Zhang F, Chen F, Fang Y, Tan W, He J, et al. Progress on structural modification of tetrandrine with wide range of pharmacological activities. Front Pharmacol. 2022; 13:978600. doi:10.3389/fphar.2022.978600.
7. Tang W, Chen J, Zhou J, Ge J, Zhang Y, Li P, et al. Quantitative MALDI imaging of spatial distributions and dynamic changes of tetrandrine in multiple organs of rats. Theranostics. 2019;9(4):932–944. doi:10.7150/thno.30408.
8. Askerova UF. Prediction of acute toxicity for (Z)-3-(2-phenylhydrazinylidene) benzofuran-2(3H)-one and its derivatives for rats using GUSAR program. New Mater Compd Appl. 2023;7(1):50-56.
9. Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Sci Rep. 2017; 7:42717. doi:10.1038/srep42717.
10. Dai CL, Xiong HY, Tang LF, Zhang X, Liang YJ, Zeng MS, et al. Tetrandrine achieved plasma concentrations capable of reversing MDR in vitro and had no apparent effect on doxorubicin pharmacokinetics in mice. Cancer Chemother Pharmacol.

2007;60(5):741-750. doi:10.1007/s00280-007-0420-0.
11. Wang F, Xu Y, Li J, Luo C, Wei M, Wu X, et al. Quantitative pulmonary pharmacokinetics of tetrandrine for SARS-CoV-2 repurposing. Front Pharmacol. 2024; 15:1457983. doi:10.3389/fphar.2024.1457983.
12. Jin H, Li L, Zhong D, Liu J, Chen X, Zheng J. Pulmonary toxicity and metabolic activation of tetrandrine in CD-1 mice. Chem Res Toxicol. 2011;24(12):2142–2152. doi:10.1021/tx2003283.
13. Shi JP, Li SX, Ma ZL, Gao AL, Song YJ, Zhang H. Acute and sub-chronic toxicity of tetrandrine in intravenously exposed female BALB/c mice. Chin J Integr Med. 2016;22(12):925-931. doi:10.1007/s11655-015-2303-2.
14. Cai Y, Qi XM, Gong LK, Liu LL, Chen FP, Xiao Y, et al. Tetrandrine-induced apoptosis in rat primary hepatocytes is initiated from mitochondria: Caspases and endonuclease G (Endo G) pathway. Toxicology. 2006;218(1):1-12. doi: 10.1016/j.tox.2005.08.024.
15. Qi XM, Miao LL, Cai Y, Gong LK, Ren J. ROS generated by CYP450, especially CYP2E1, mediate mitochondrial dysfunction induced by tetrandrine in rat hepatocytes. Acta Pharmacol Sin. 2013; 34(9):1229–1236. doi:10.1038/aps.2013.71.

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